

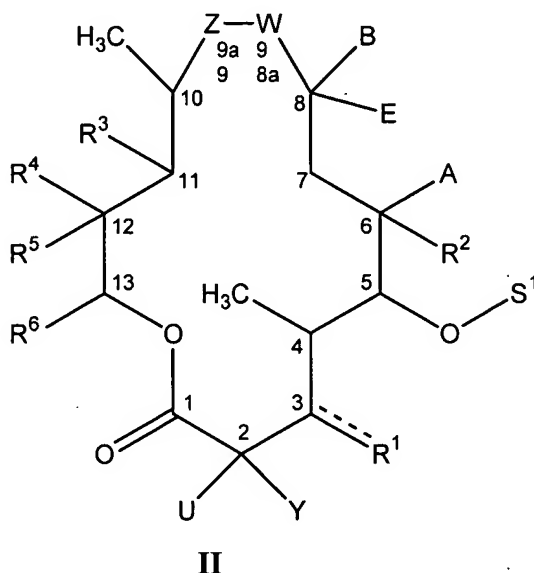
AMENDMENTS TO THE CLAIMS

1. (Previously presented) A compound of the formula:



I

wherein **M** represents a group of Formula II:



wherein

(i) Z and W independently are  $>C=O$ ,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$  or  $>C=N-R_M$ , wherein

$R_t$  and  $R_s$  independently are hydrogen or alkyl;

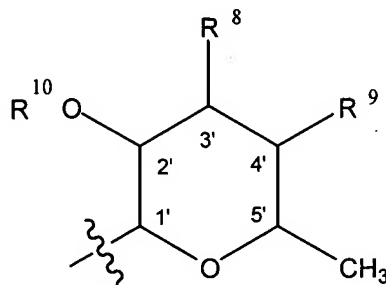
$R_M$  is hydroxy, alkoxy, substituted alkoxy or  $OR^p$ ;

$R_N$  is hydrogen,  $R^p$ , alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or  $-C(X)-NR_tR_s$ ; wherein X is  $=O$  or  $=S$ ;

provided that Z and W cannot both simultaneously be,  $>C=O$ ,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$ ,  $>C=N-R_M$  or a bond;

(ii) U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

- (iii) R<sup>1</sup> is hydroxy, OR<sup>p</sup>, -O-S<sup>2</sup> group or an =O;  
(iv) S<sup>1</sup> is a sugar moiety of Formula III:



### III

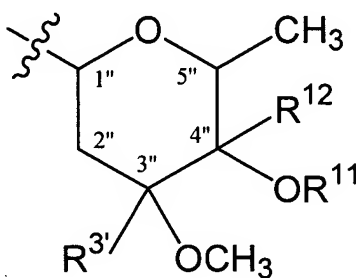
wherein

R<sup>8</sup> and R<sup>9</sup> are both hydrogen or together form a bond, or R<sup>9</sup> is hydrogen and R<sup>8</sup> is -N(CH<sub>3</sub>)R<sup>y</sup>, wherein

R<sup>y</sup> is R<sup>p</sup>, R<sup>z</sup> or -C(O)R<sup>z</sup>, wherein R<sup>z</sup> is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with C<sub>2</sub>-C<sub>7</sub>-alkyl, C<sub>2</sub>-C<sub>7</sub>-alkenyl, C<sub>2</sub>-C<sub>7</sub>-alkynyl, aryl or heteroaryl;

$R^{10}$  is hydrogen or  $R^p$ ;

S<sup>2</sup> sugar moiety of Formula IV:



IV

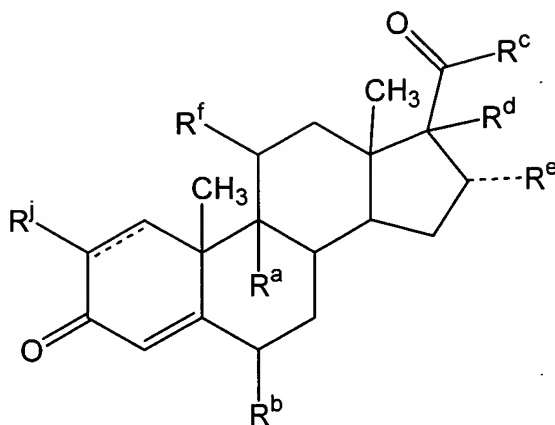
wherein

R<sup>3'</sup> is hydrogen or methyl;

R<sup>11</sup> is hydrogen, R<sup>p</sup>, or O-R<sup>11</sup> is a group that with R<sup>12</sup> and with C/4" carbon atom forms a >C=O or epoxy group;

R<sup>12</sup> is hydrogen or a group that with O-R<sup>11</sup> group and with C/4" carbon



**X**

wherein

$R^a$  and  $R^b$  independently represents, hydrogen or halogen;

$R^c$  is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

$R^d$  and  $R^e$  independently represents: hydrogen, hydroxy, methyl or  $C_1$ - $C_4$ -alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

$R^f$  is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

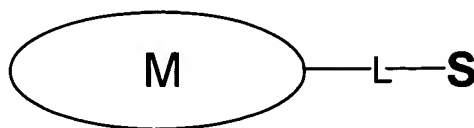
$R^j$  is hydrogen or halogen;

or a pharmaceutically acceptable salt or solvate thereof;

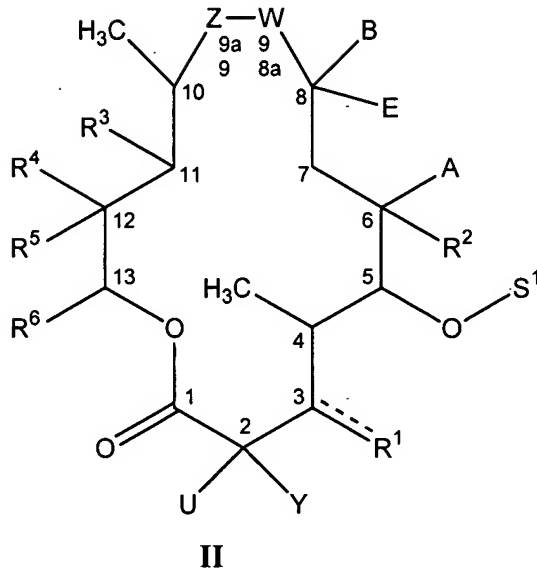
wherein

L is a linker molecule to which each of M and S are covalently linked.

2. (Currently amended) A compound of the Formula I:

**I**

wherein **M** represents a group of Formula II:



wherein

(i) Z and W independently are  $>C=O$ ,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$  or  $>C=N-R_M$ , wherein

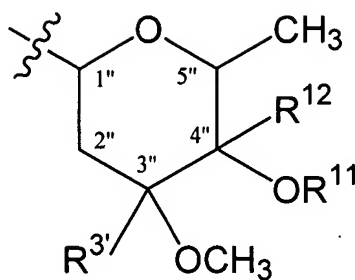
$R_t$  and  $R_s$  independently are hydrogen or alkyl;

$R_M$  is hydroxy, alkoxy, substituted alkoxy or  $OR^p$ ;

$R_N$  is hydrogen,  $R^p$ , alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or  $-C(X)-NR_tR_s$ ; wherein X is  $=O$  or  $=S$ ;

provided that Z and W cannot both simultaneously be,  $>C=O$ ,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$ ,  $>C=N-R_M$  or a bond;





IV

wherein

R<sup>3'</sup> is hydrogen or methyl;

R<sup>11</sup> is hydrogen, R<sup>p</sup>, or O-R<sup>11</sup> is a group that with R<sup>12</sup> and with C/4" carbon atom forms a >C=O or epoxy group;

R<sup>12</sup> is hydrogen or a group that with O-R<sup>11</sup> group and with C/4" carbon atom forms a >C=O or epoxy group;

(vi)  $R^2$  is hydrogen, hydroxy,  $OR^p$  or alkoxy ;

(vii) A is hydrogen or methyl;

(viii) B is methyl or epoxy;

(ix) E is hydrogen or halogen;

R<sup>3</sup> is hydroxy, OR<sup>p</sup>, alkoxy or R<sup>3</sup> is a group that with R<sup>5</sup> and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is >N-R<sub>N</sub> R<sup>3</sup> is a group that with W or Z forms a cyclic carbamate;

(xi)  $R^4$  is C<sub>1</sub>-C<sub>4</sub> alkyl;

(xii) R<sup>5</sup> is hydrogen, hydroxy, OR<sup>p</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy, or a group that with R<sup>3</sup> and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;

(xiii)  $R^6$  is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl;

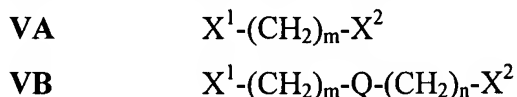
wherein **M** has a linkage site through which it is linked to **S** *via* linking group **L**; provided that the linkage site being at one or more of the following:

- any reactive hydroxy, nitrogen, or epoxy group located on  $S^1$ ,  $S^2$ , or an aglycone oxygen if  $S^1$  and/or  $S^2$  is cleaved off;
- a reactive  $>N-R_N$  or  $-NR_4R_5$  or oxo group located on Z or W;
- a reactive hydroxy group located at any one of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^5$ ;

d) any other group that can be first derivatized to a hydroxy or -NR<sub>t</sub>R<sub>s</sub> group and

R<sup>p</sup> is hydroxyl or amino protective group; and

**L represents a group of Formula VA or of Formula VB:**



wherein

X<sup>1</sup> is selected from: -CH<sub>2</sub>-, -CH<sub>2</sub>NH-, -C(O)-, -OC(O)-, =N-O- or -OC(O)NH-;

-C(O)NH;

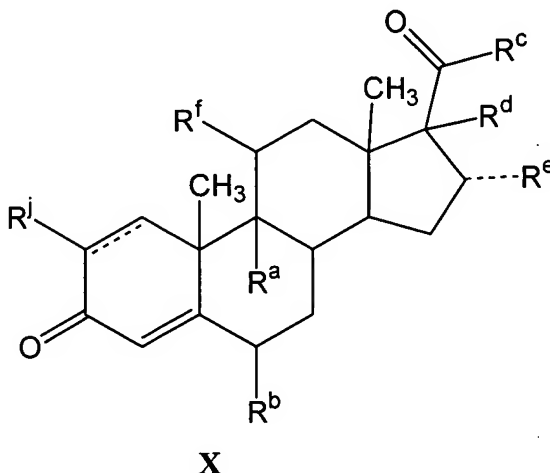
X<sup>2</sup> is -NH- or -NHC(O)- or -CH<sub>2</sub>-;

Q is -NH- or -CH<sub>2</sub>-, wherein

each -CH<sub>2</sub>- or -NH- group may be optionally substituted by C<sub>1</sub>-C<sub>7</sub>-alkyl, C<sub>2</sub>-C<sub>7</sub>-alkenyl, C<sub>2</sub>-C<sub>7</sub>-alkynyl, C(O)R<sup>x</sup>, C(O)OR<sup>x</sup>, C(O)NHR<sup>x</sup>, wherein R<sup>x</sup> may be C<sub>1</sub>-C<sub>7</sub>-alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 8, with the proviso that if Q is NH, n cannot be 0;

S represents a group of Formula X:



wherein

R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;



$R^c$  is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;  
 $R^d$  and  $R^e$  independently represents: hydrogen, hydroxy, methyl or  $C_1$ - $C_4$ -alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;  
 $R^f$  is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;  
 $R^j$  is hydrogen or halogen;  
or a pharmaceutically acceptable salt or solvate thereof.

3. (Canceled).
4. (Canceled)
5. (Previously presented) The compound according to claim 2 wherein  
Z is  $>NR_N$ , wherein  $R_N$  is hydrogen or a methyl group;  
W is  $>CH_2$ ;  
B is methyl;  
E is hydrogen;  
 $R^2$  is hydroxy;  
A is methyl;  
 $S^1$  group represents a group of Formula **III** wherein  
 $R^8$  is selected from: hydrogen, amino, *N*-methylamino, *N,N*-dimethylamino,  
*N*-methyl-*N*-( $C_2$ - $C_4$ )-alkylamino, *N*-methyl-*N*-methylcarbonylamino,  
*N*-methyl-*N*-benzylamino, *N*-methyl-*N*-cyclohexylamino;  
 $R^9$  and  $R^{10}$  are hydrogen;  
 $R^1$  is  $O-S^2$  wherein  $S^2$  represents a group of Formula **IV** wherein  $R^{11}$  and  $R^{12}$  are hydrogen and  $R^{13}$  is methyl;  
U is hydrogen;  
Y is methyl;



$R^5$  is hydroxy or methoxy;

$R^6$  is ethyl;

provided that the linkage is through the nitrogen of  $R^8$  at C/3', through the oxygen of  $R^2$  at C/6 or through the carbon of  $R^{12}$  or through the oxygen of  $R^{11}$  both at C/4".

7. (Previously presented) The compound according to claim 2 wherein

$R^a$  and  $R^b$  independently represents, hydrogen or halogen;

$R^d$  is hydrogen or hydroxy;

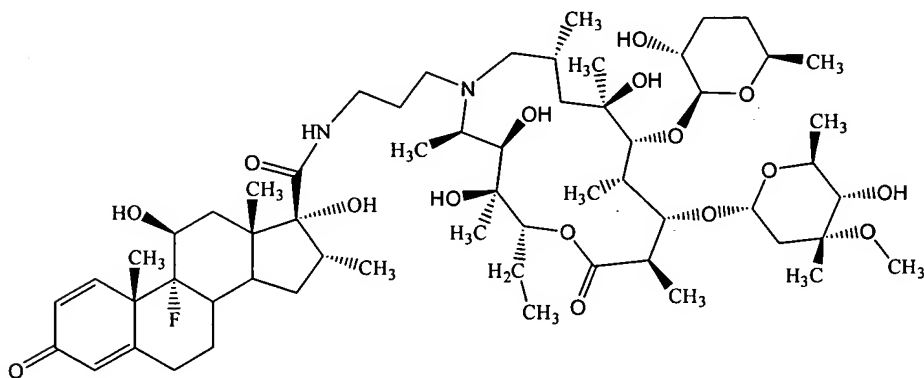
$R^e$  is methyl;

$R^f$  is hydroxy;

$R_j$  is hydrogen

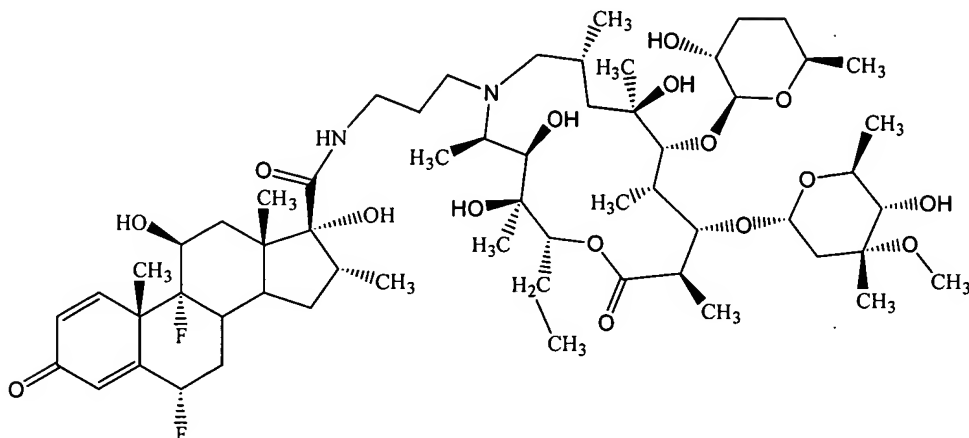
provided that the linkage is through the valence bond  $R^k$ .

8. (Currently amended) A compound of the formula



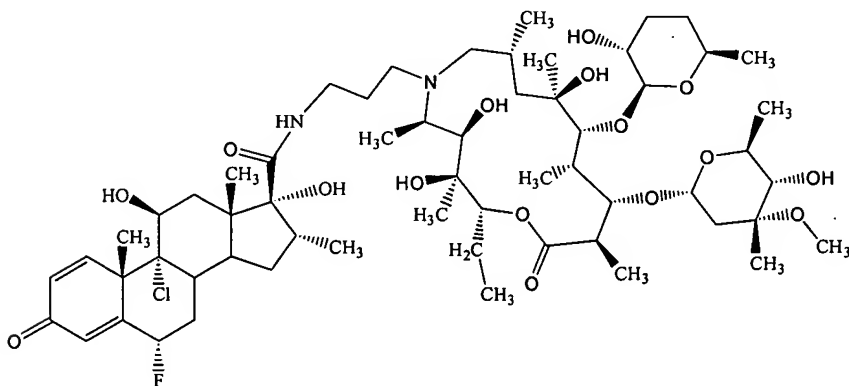
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

9. ((Currently amended)) A compound of the formula



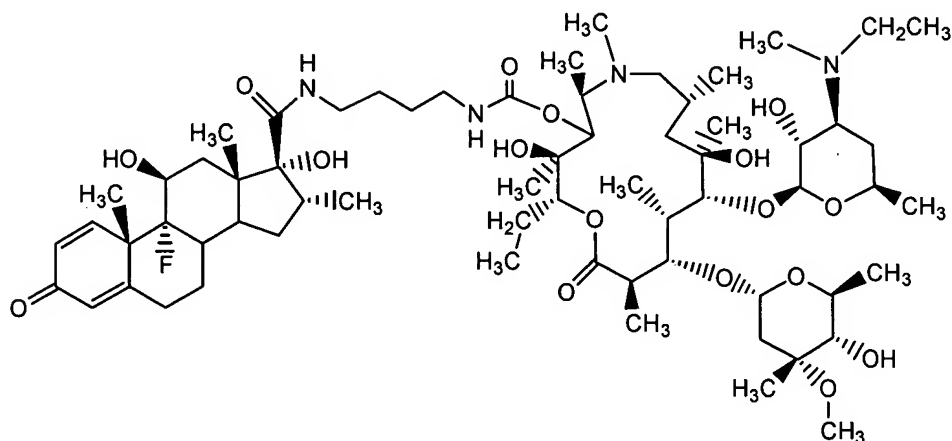
~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof.

10. (Currently amended) A compound of the formula



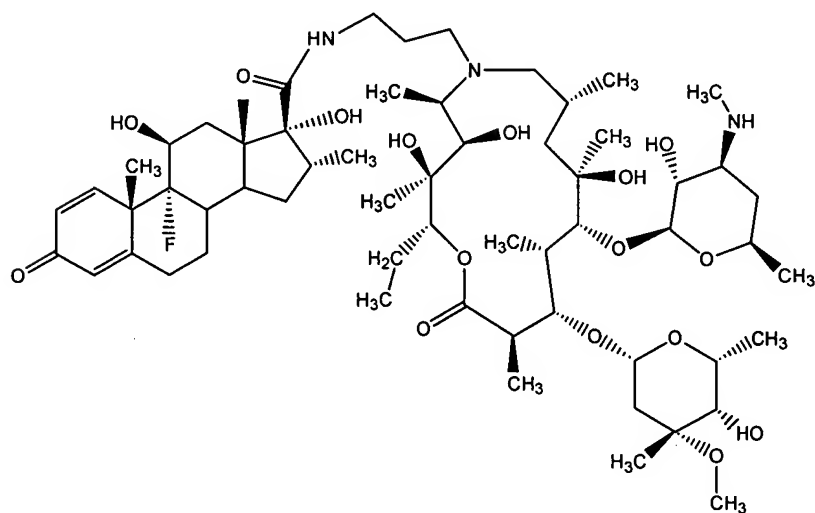
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

11. (Currently amended) A compound of the formula



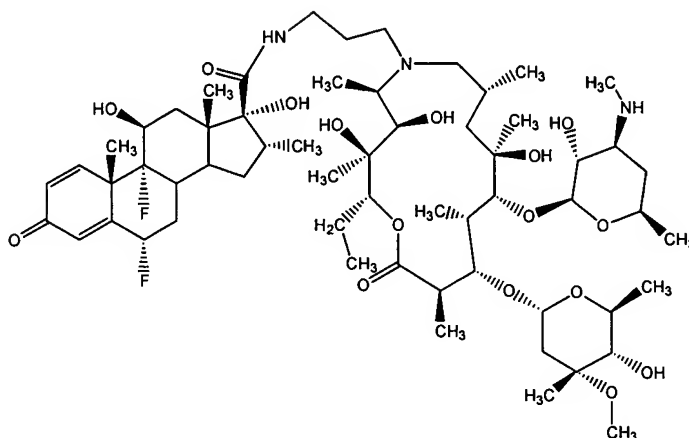
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

12. (Currently amended) A compound of the formula



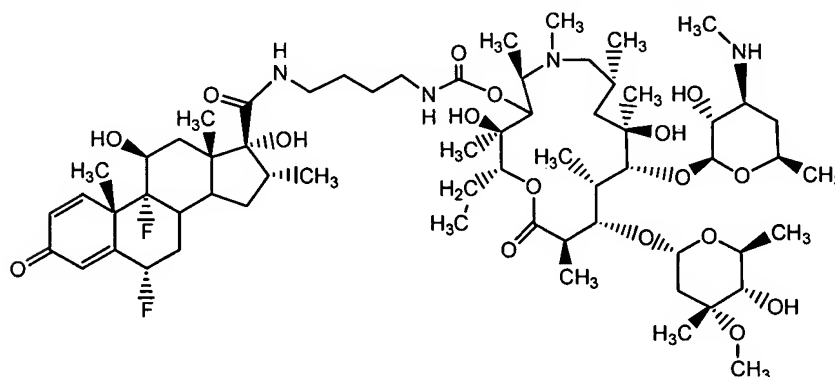
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

13. (Currently amended) A compound of the formula



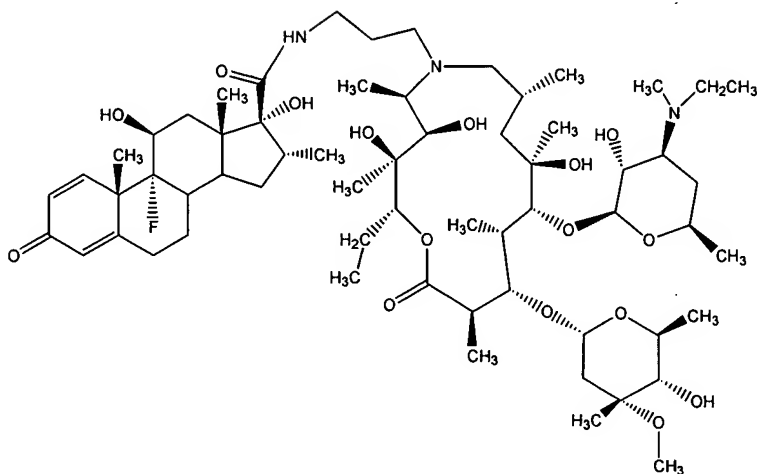
~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof.

14. (Currently amended) A compound of the formula



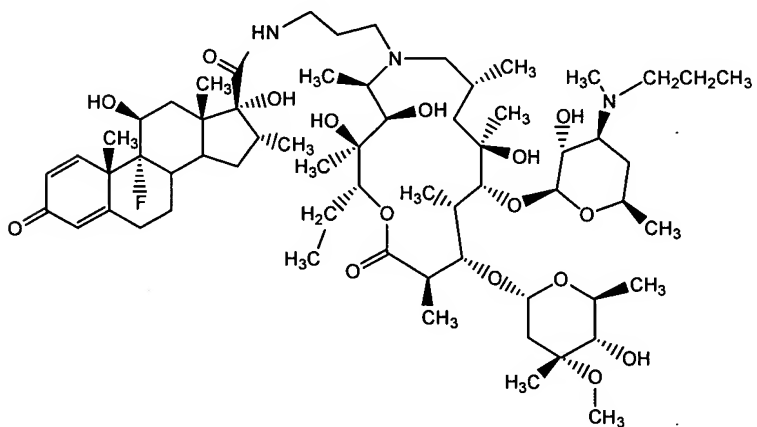
~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof.

15. (Currently amended) A compound of the formula



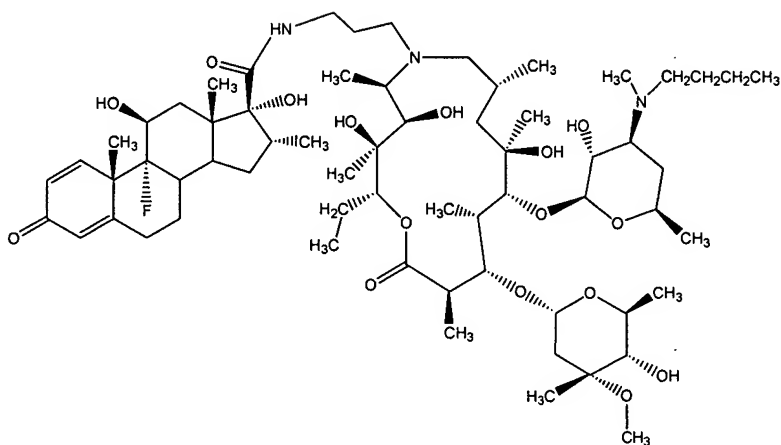
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

16. (Currently amended) A compound of the formula



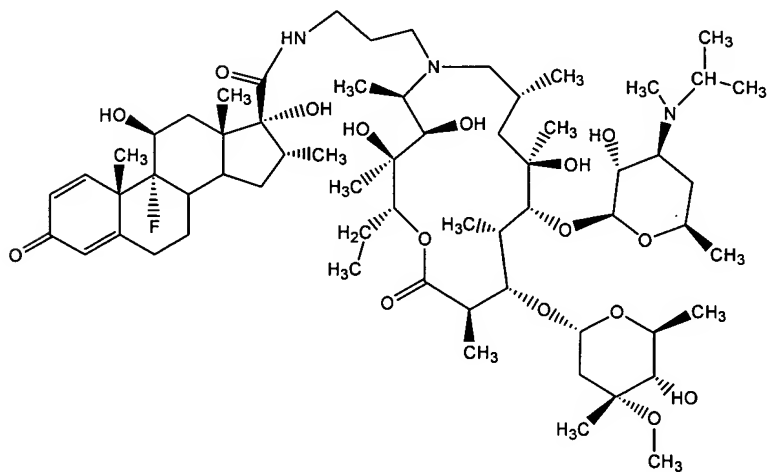
~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof..

17. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

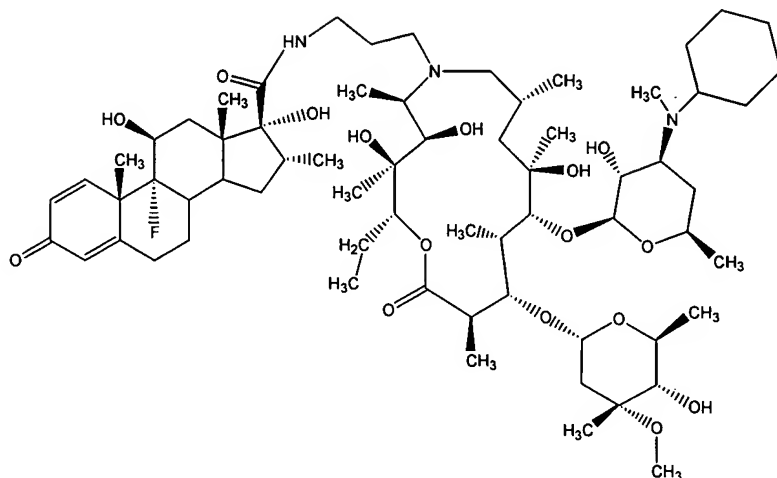
18. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

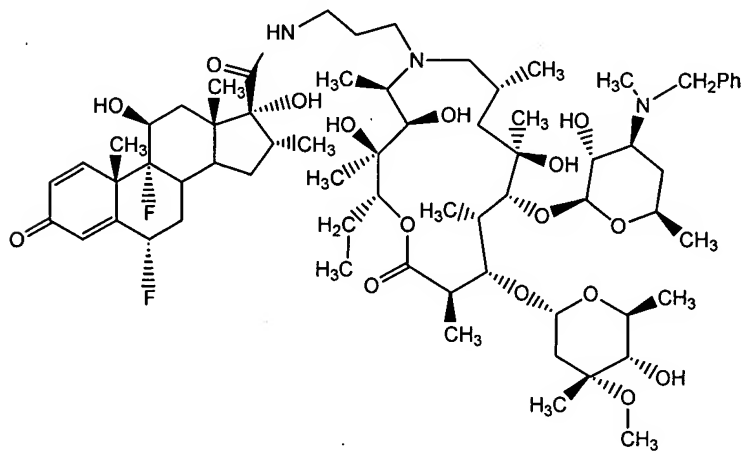


19. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof or a~~  
pharmaceutically acceptable salt or solvate thereof.

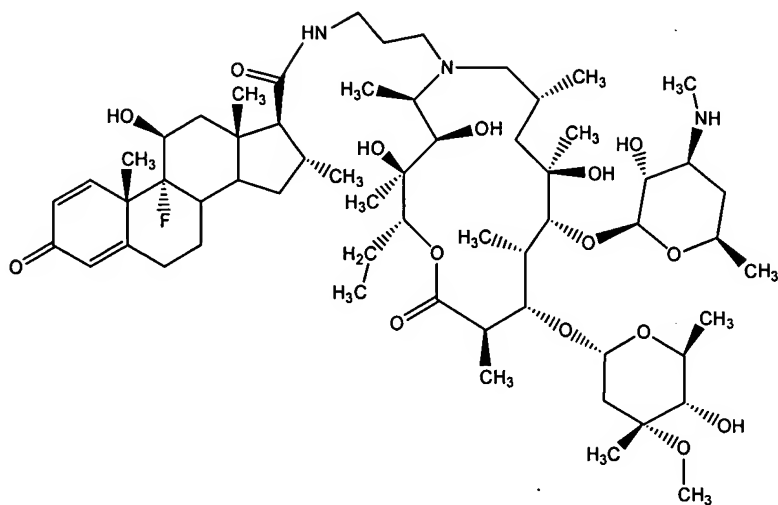
20. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof or a~~  
pharmaceutically acceptable salt or solvate thereof..

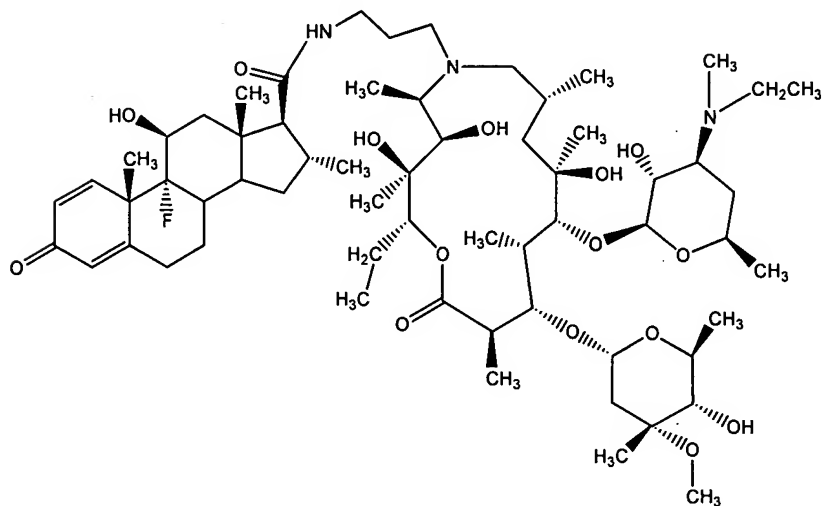


23. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

24. (Currently amended) A compound of the formula



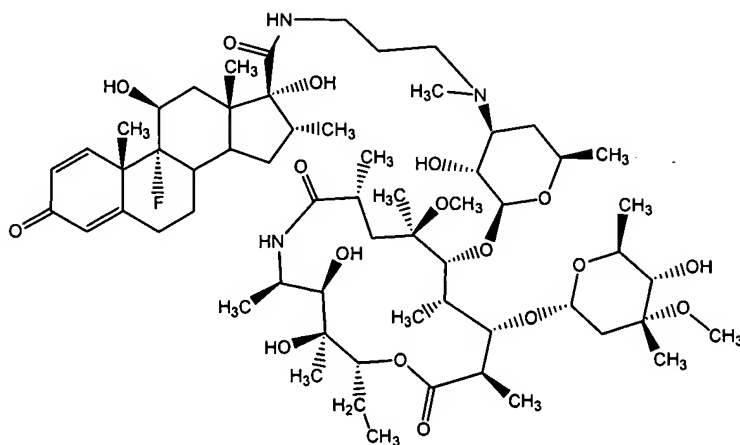
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.





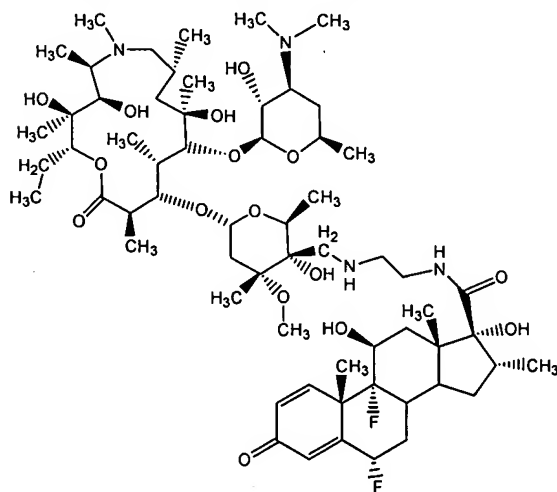


31. (Currently amended) A compound of the formula



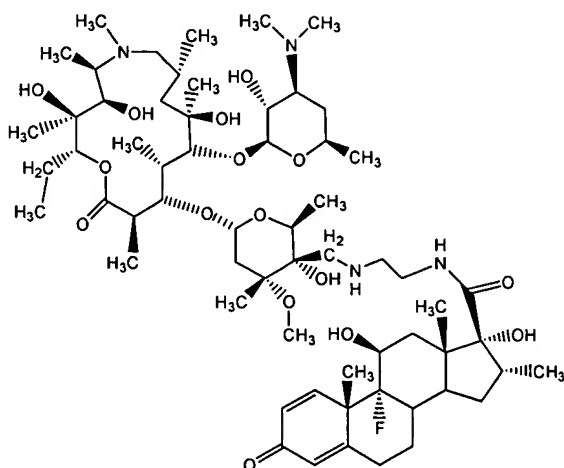
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

32. (Currently amended) A compound of the formula



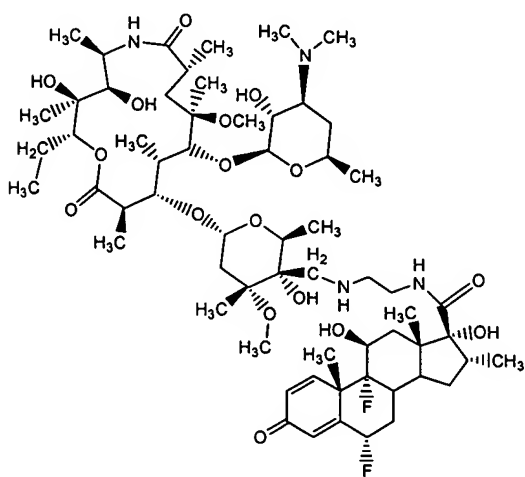
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

33. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

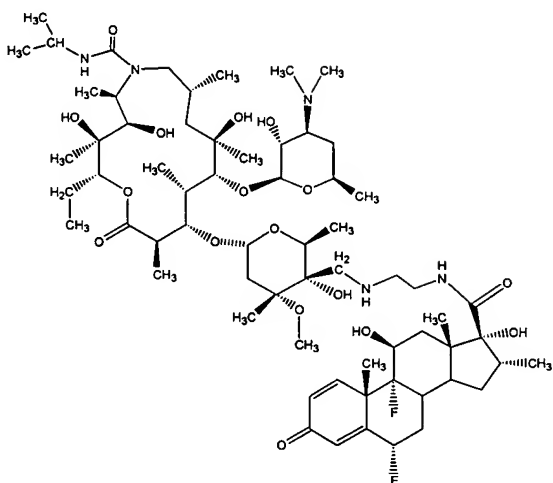
34. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof.

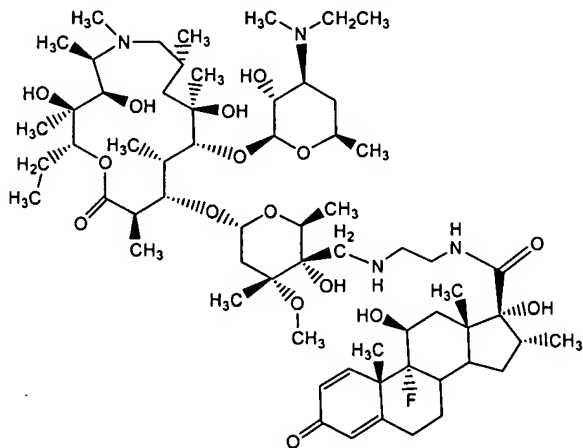


35. (Currently amended) A compound of the formula



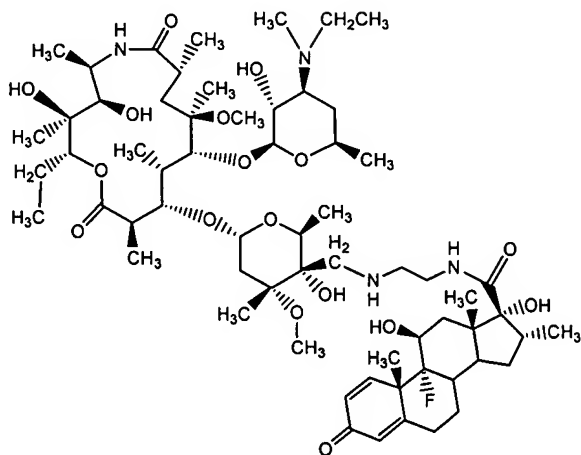
~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof.

36. (Currently amended) A compound of the formula



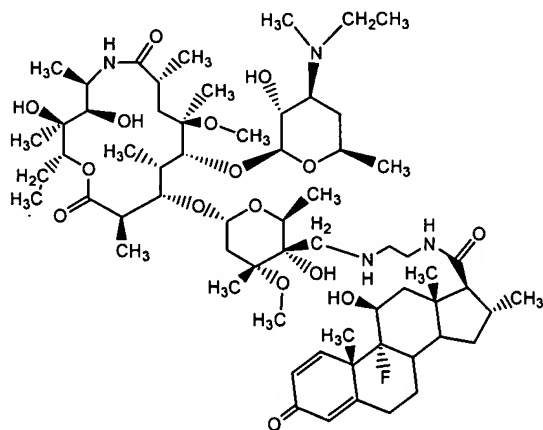
~~and pharmaceutically acceptable salts and solvates thereof~~ or a  
pharmaceutically acceptable salt or solvate thereof.

37. (Currently amended) A compound of the formula



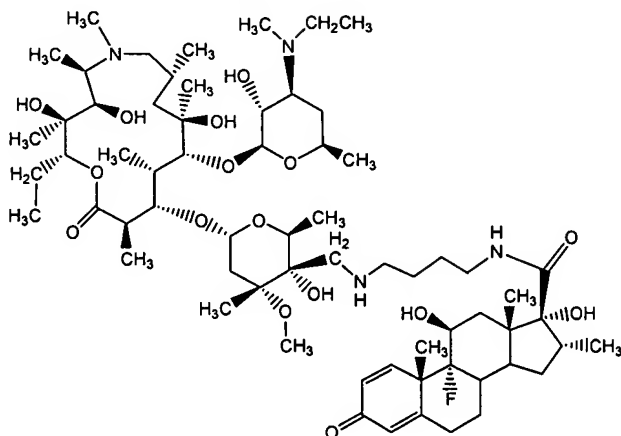
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

38. (Currently amended) A compound of the formula



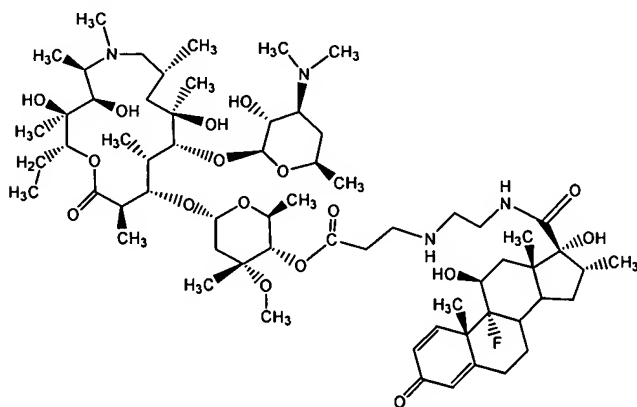
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

39. (Currently amended) A compound of the formula



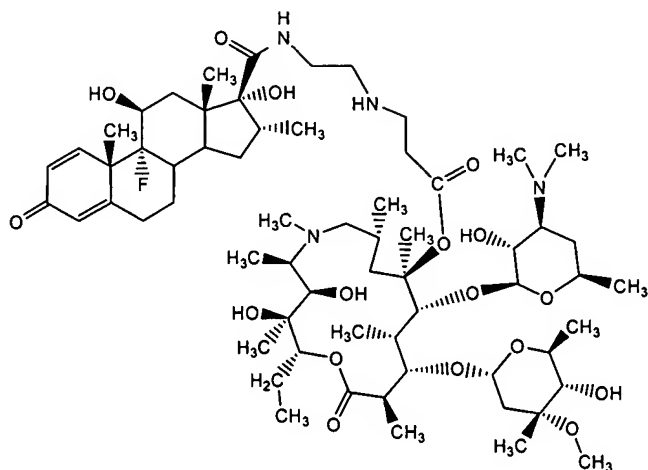
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

40. (Currently amended) A compound of the formula



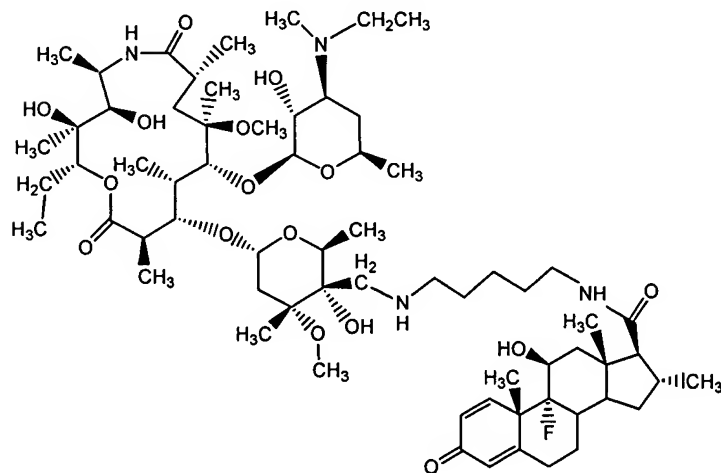
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

41. (Currently amended) A compound of the formula



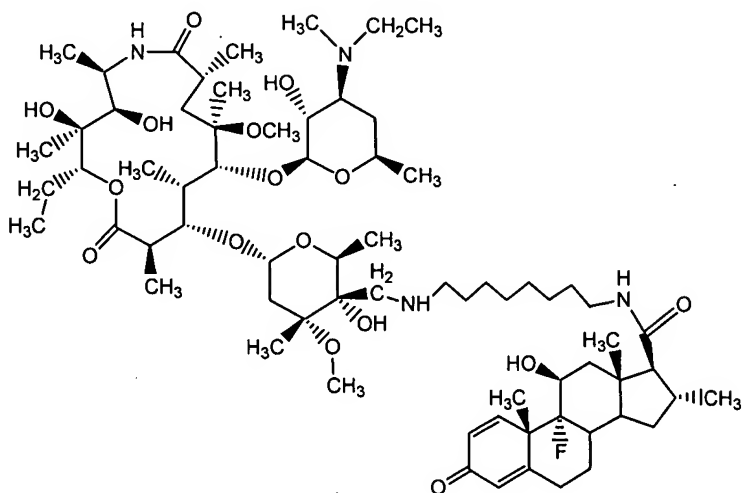
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

42. (Currently amended) A compound of the formula



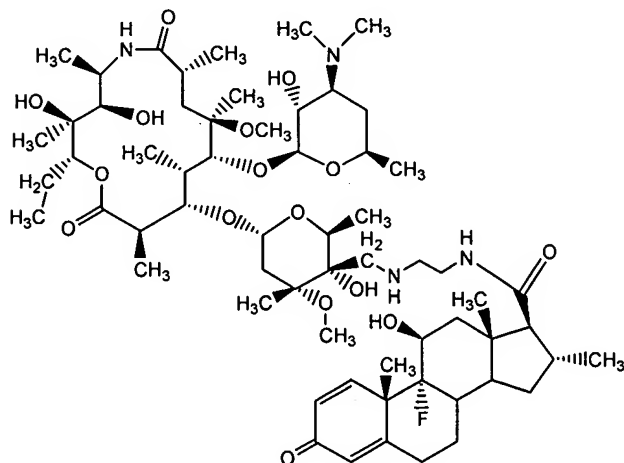
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

43. (Currently amended) A compound of the formula



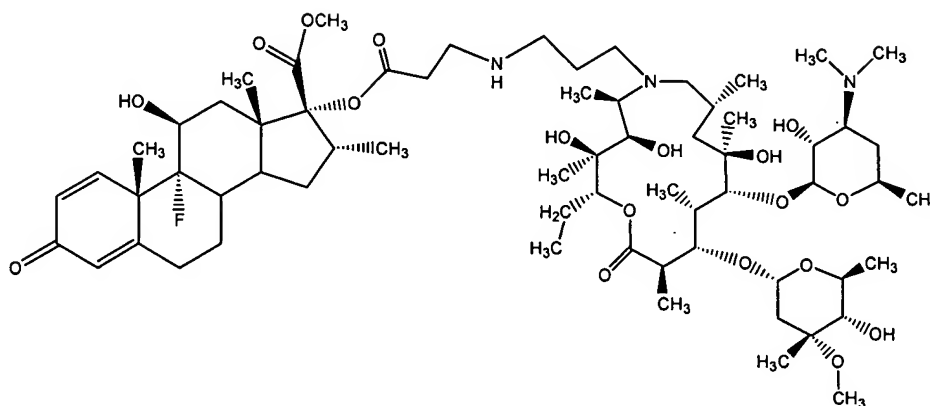
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

44. (Currently amended) A compound of the formula



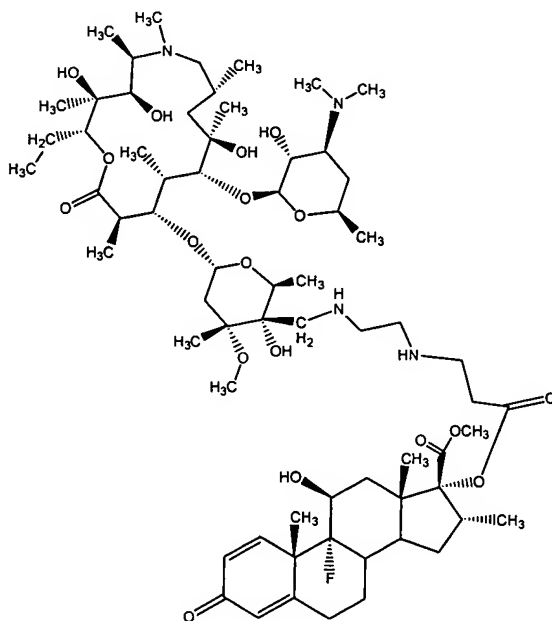
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

45. (Currently amended) A compound of the formula



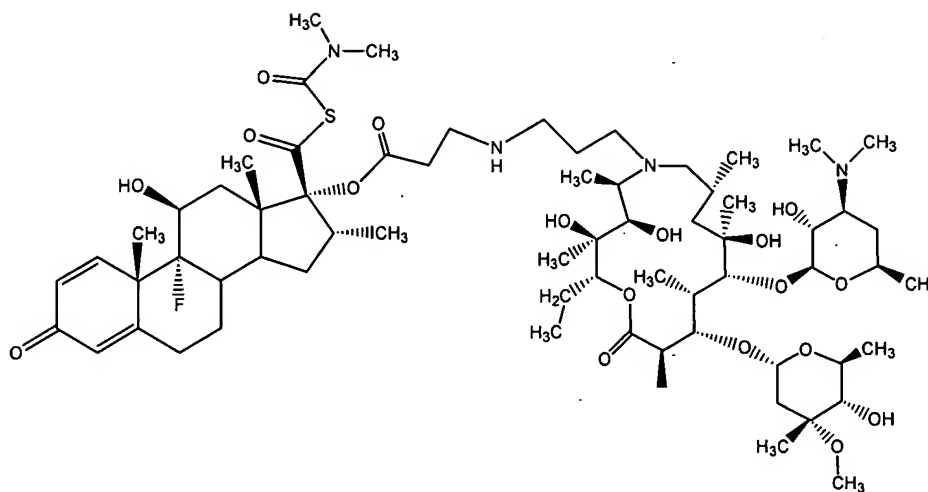
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

46. (Currently amended) A compound of the formula



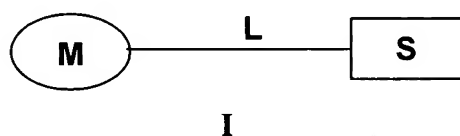
~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

47. (Currently amended) A compound of the formula



~~and pharmaceutically acceptable salts and solvates thereof~~ or a pharmaceutically acceptable salt or solvate thereof.

48. (Currently amended) A process for the preparation for a compound of Formula I:



wherein **M** represents a group of Formula II:





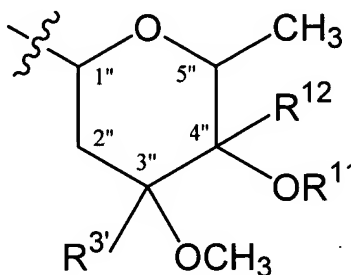
wherein

$R^8$  and  $R^9$  are both hydrogen or together form a bond, or  $R^9$  is hydrogen and  $R^8$  is  $-N(CH_3)R^y$ , wherein

$R^y$  is  $R^p$ ,  $R^z$  or  $-C(O)R^z$ , wherein  $R^z$  is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with  $C_2$ - $C_7$ -alkyl,  $C_2$ - $C_7$ -alkenyl,  $C_2$ - $C_7$ -alkynyl, aryl or heteroaryl;

$R^{10}$  is hydrogen or  $R^p$ ;

$S^2$  sugar moiety of Formula IV:



IV

wherein

$R^{3'}$  is hydrogen or methyl;

$R^{11}$  is hydrogen,  $R^p$ , or  $O-R^{11}$  is a group that with  $R^{12}$  and with C/4'' carbon atom forms a  $>C=O$  or epoxy group;

$R^{12}$  is hydrogen or a group that with  $O-R^{11}$  group and with C/4'' carbon atom forms a  $>C=O$  or epoxy group;

(vi)  $R^2$  is hydrogen, hydroxy,  $OR^p$  or alkoxy ;

(vii) A is hydrogen or methyl;

(viii) B is methyl or epoxy;

(ix) E is hydrogen or halogen;

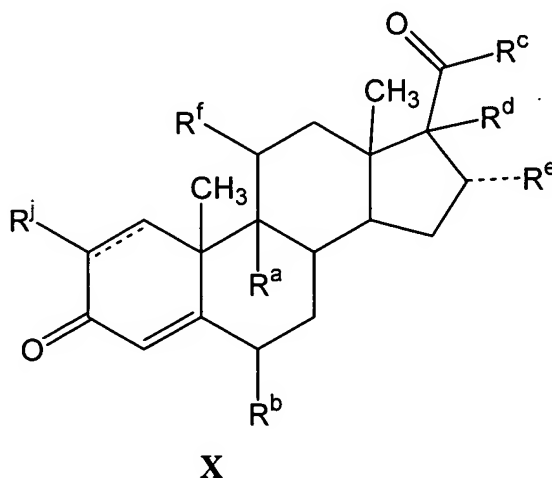
$R^3$  is hydroxy,  $OR^p$ , alkoxy or  $R^3$  is a group that with  $R^5$  and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is  $>N-R_N$   $R^3$  is a group that with W or Z forms a cyclic carbamate;

(xi)  $R^4$  is  $C_1$ - $C_4$  alkyl;

(xii)  $R^5$  is hydrogen, hydroxy,  $OR^p$ ,  $C_1$ - $C_4$  alkoxy, or a group that with  $R^3$



~~L is a linker molecule to which each of M and S are covalently linked.~~



wherein

R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;

R<sup>c</sup> is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

R<sup>d</sup> and R<sup>e</sup> independently represents: hydrogen, hydroxy, methyl or C<sub>1</sub>-C<sub>4</sub>-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

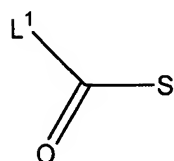
R<sup>f</sup> is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

$R^j$  is hydrogen or halogen;

or a pharmaceutically acceptable salt or solvate;

a) for a compound represented by Formula I comprising the steps of:

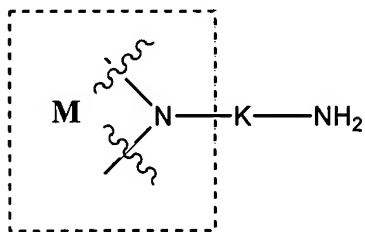
where X<sup>2</sup> is -NHC(O)-, by reacting a compound of Formula V:



V

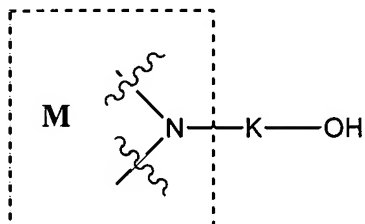
wherein L<sup>1</sup> represents a leaving group, and a free amino group of a macrolide

represented by Formula **VIId**:



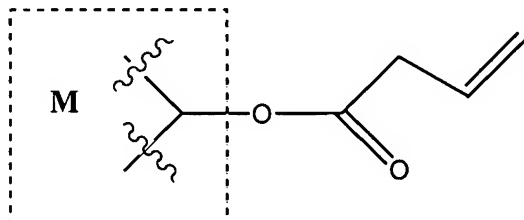
**VIId**

b) for a compound represented by Formula **I**, where  $X^2$  is  $-\text{OC}(\text{O})-$ , by reacting a compound of Formula **V** and a hydroxyl group of a macrolide represented by Formula **VIe**:

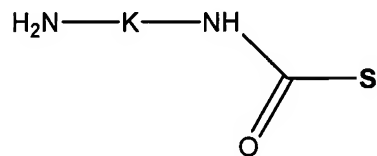


**VIe**

c) for a compound represented by Formula **I**, wherein  $X^1$  is  $-\text{OC}(\text{O})-$ ,  $Q$  is  $\text{NH}$  and  $X^2$  is  $-\text{NHC}(\text{O})-$ , by reacting a macrolide represented by:



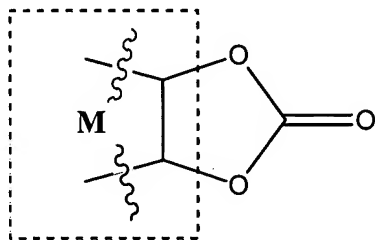
and a free amino group of the compound represented by Formula **IVc**:



**IVc**

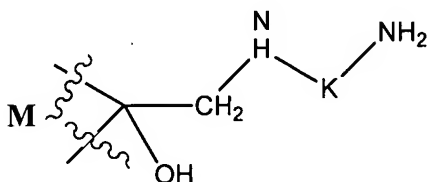
d) for a compound represented by Formula **I**, where  $X^1$  is  $-\text{OC}(\text{O})\text{NH}-$  and  $X^2$  is  $-\text{NHC}(\text{O})-$ , by reacting a macrolide represented by Formula **VII** and

a free amino group of Formula **IVc**:



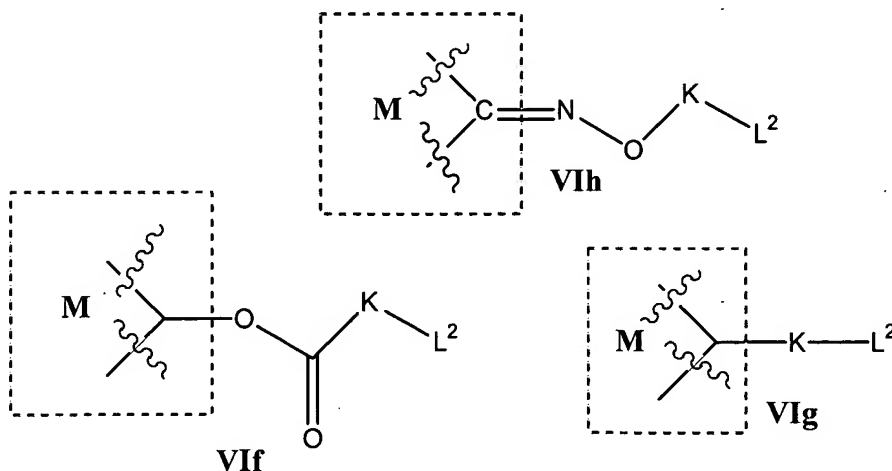
## VII

e) for a compound represented by Formula **I**,  $X^1$  is  $-\text{CH}_2-$ ,  $Q$  is  $-\text{NH}-$  and  $X^2$  is  $-\text{NHC(O)}-$ , by reacting a macrolide represented by Formula **Va** and a compound of Formula **V**:

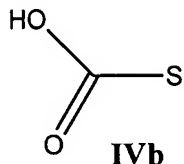


Va

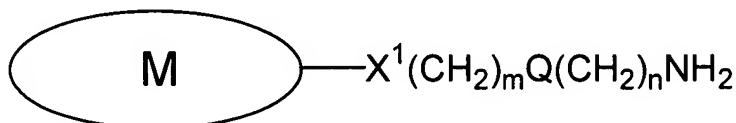
f) compound of Formula **I** by reacting a macrolide represented by Formula **VIh** or by Formula **VIg** or by Formula **VIi** having a leaving group  $L^2$



with a free carboxyl acid of steroid represented by Formula **IVb**

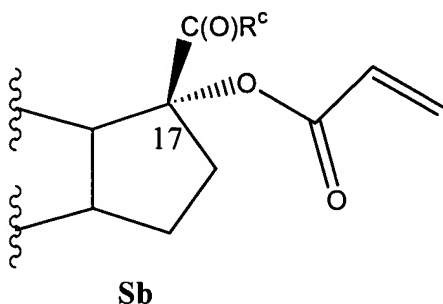


g) for a compound represented by Formula I, wherein X<sup>1</sup> is -OC(O)-, Q is NH and X<sup>2</sup> is -NH- by reacting a macrolide represented by:



VId

and a steroid subunit having a  $-C=C-$  bond represented by Formula **Sb**:



following by modification of  $R^c$  group.

49. (Currently Amended) A pharmaceutical composition comprising a compound according to claim 1 ~~and~~ or a pharmaceutically acceptable ~~salts~~ salt or solvate thereof as well as pharmaceutically acceptable diluent or carrier.
50. (Currently Amended) A method of treatment of inflammatory diseases, disorders ~~and~~ or conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF- $\alpha$  and IL-1 which comprises administering to a subject in need of treatment a therapeutically effective amount of a compound according to claim 1.



